1. NAME OF THE MEDICINAL PRODUCT

Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14 Valent)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Single Dose (0.5 mL) Presentation:

Each dose of 0.5 mL contains:

Pneumococcal polysaccharide serotype 1	:	3.0 µg
Pneumococcal polysaccharide serotypes 3, 4, 5, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F	:	2.2 µg
Pneumococcal polysaccharide serotype 6B	:	4.4 µg
Adsorbed onto Aluminum Phosphate, as Al^{+++}	:	≤ 0.75 mg

Polysaccharides conjugated to 20-50 µg of CRM_{197}

Multi Dose (2.5 mL) Presentation:

Each dose of 0.5 mL contains:

Pneumococcal polysaccharide serotype 1	:	3.0 µg
Pneumococcal polysaccharide serotypes 3, 4, 5, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F	:	2.2 µg
Pneumococcal polysaccharide serotype 6B	:	4.4 µg
Adsorbed onto Aluminum Phosphate, as Al^{+++}	:	≤ 0.75 mg
2- Phenoxyethanol	:	4 mg

Polysaccharides conjugated to 20-50 µg of CRM_{197}

3. PHARMACEUTICAL FORM

BE-PCV14 is a whitish suspension in which the mineral carriers tend to settle down slowly. The vaccine contains *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F. These polysaccharides are conjugated using CRM_{197}. The antigens are adsorbed onto Aluminum Phosphate as an adjuvant. 2 Phenoxyethanol is used as preservative only in Multi-dose Presentation.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

BE-PCV14 is indicated for active immunization against invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in children from 6 weeks of age.

4.2 Posology and Method of Administration

BE-PCV14 is to be administered as a three dose primary series in infants at 6-10-14 weeks. The vaccine should be administered intramuscularly. The preferred site is anterolateral aspect of the upper thigh. The vaccine should not be injected in the gluteal area. The vaccine should not be injected intradermally, subcutaneously or intravenously since the safety and immunogenicity of these routes have not been evaluated.

4.3 Contraindications

Hypersensitivity to any constituents of the vaccine listed in section 6.1

4.4 Special Warning and Precautions for Use

- Do not administer intravenously, intradermally, or subcutaneously.
- Like all other vaccines, supervision and appropriate medical treatment should always be available to treat any anaphylactic reactions following immunization
- **The vaccinee should remain under medical supervision for at least 30 minutes after vaccination**
- Concurrent illness: As with other vaccines, administration of BE-PCV14 should be postponed in individuals suffering from an acute severe febrile illness.
- Adrenaline Injection (1:1000) should be available in case of acute Anaphylactic reaction following vaccination.
- **Thrombocytopenia and coagulation disorders:** As with any other intramuscular injection, BE-PCV14 should be given with caution in individuals with

thrombocytopenia and coagulation disorders or to individuals on treatment with anticoagulation therapy, because of risk of bleeding or bruising following an intramuscular injection in these individuals

- **Immunocompromised individuals:** It is not known if individuals with impaired immune responsiveness, including individuals receiving immunosuppressant therapy, will elicit the same response as immunocompetent individuals to BE-PCV14. These individuals may have a weaker immune response to the vaccine

BE-PCV 14 should be shaken well to obtain a uniform, whitish translucent suspension before use. Prior to administration, the vaccine vial should be visually checked for complete suspension and presence of any particulate matter or other coloration, if any doubt, do not use the contents of the vial. Sterile needle and syringe should be used for withdrawal of the vaccine.

4.5 Drug interactions

BE-PCV14 can be given with either monovalent or combination vaccines containing diphtheria, tetanus, whole-cell pertussis, hepatitis B, *Haemophilus influenzae* type b, inactivated or oral poliomyelitis and rotavirus vaccine. Clinical studies demonstrated that the safety profiles of the administered vaccines were unaffected. For concomitant administration, use different injection sites and separate syringes.

4.6 Use in Special Populations (such as pregnant women, lactating women)

Safety and effectiveness have not been established in pregnant women, nursing mothers. It is not known whether the vaccine is excreted in human milk.

4.7 Effect on Ability to Drive and Use Machines

No studies on the effect of BE-PCV14 on the ability to drive and use machines have been performed.

4.8 Undesirable Effects

Clinical Trial Experience: The safety of BE's Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed) (14 Valent) was established in 6–8-week-old infants, 12-23 months old toddlers and 18–45-year-old adult individuals. Within each system organ class (SOC) the adverse reactions were ranked under headings using the following convention:

Very common	≥ 10%
Common	≥ 1% and < 10%
Uncommon	≥ 0.1% and < 1%
Rare	≥ 0.01% and < 0.1%
Very rare	< 0.01%

Systemic:

Common (≥ 1% and < 10%)

- Fever/Pyrexia
- Irritability Post vaccinal
- Decreased Appetite

Uncommon (≥ 0.1% and < 1%)

- Diarrhea
- Vomiting
- Somnolence

Local:

Very common (≥ 10%)

- Injection site pain (tenderness)

Common (≥ 1% and < 10%)

- Injection site erythema
- Injection site induration/swelling

Summary of safety profile: In a Phase-I (BECT043) study conducted in 24 subjects aged ≥18 to ≤45 years, the most frequently reported local adverse events were injection site pain, injection site erythema, and injection site pain (tenderness). All injection site reactions were considered as vaccine related. The most frequently reported systemic

adverse events were chills, headache, pyrexia and rash. All the systemic AEs reported were judged to be related to the study vaccination by the principal investigator.

In Phase-II (BECT044) study conducted in 120 subjects aged 12–23-month-old, healthy Indian PCV-naïve toddlers, randomized in 1:1 ratio between BE-PCV14 or 13 valent licensed comparator, the most common Treatment emergent AEs by preferred term reported in BE-PCV14 group were Injection site pain, pyrexia, injection site swelling, injection site erythema/redness, crying and decreased appetite.

In a controlled Phase-III (BECT051) study conducted in 1290 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13 valent licensed comparators, the safety profile of BE-PCV14 was comparable to the licensed PCV in terms of overall AE rates, related AE rates and medically attended AEs. The total number of subjects with at least one adverse event reported in BE-PCV14 group were 175/645 (27.1%) as against 178/645 (27.6%) in the licensed comparator group. The number of subjects reporting at least one adverse event were similar in BE-PCV14 and licensed comparator groups. Out of total 1290 enrolled subjects, 175/645 (27.1%) subjects reported 355 events and 178/645 (27.6%) subjects reported 353 events in BE-PCV14 and licensed comparator groups respectively. The most commonly reported adverse events in BE-PCV14 group were Injection site pain [133 AEs in 93 (14.4%) subjects], Pyrexia [53 AEs in 42 (6.5%) subjects], Injection site swelling [51 AEs in 44 (6.8%) subjects], Injection site erythema [38 AEs in 33 (5.1%) subjects], Irritability postvaccinal [41 AEs in 25 (3.9%) subjects], Injection site induration [13 AEs in 9 (1.4%) subjects], Decreased appetite [9 AEs in 8 (1.2%) subjects], Diarrhoea [8 AEs in 6 (0.9%) subjects], Vomiting [3 AEs in 3 (0.5%) subjects] and Somnolence [4 AEs in 2 (0.3%) subjects]. The most commonly reported adverse events in licensed comparator group were Injection site pain [131 AEs in 98 (15.2%) subjects], Pyrexia [51 AEs in 40 (6.2%) subjects], Injection site swelling [58 AEs in 48 (7.4%) subjects], Injection site erythema [44 AEs in 36 (5.6%) subjects], Irritability post vaccinal [31 AEs in 21 (3.3%) subjects], Injection site induration [18 AEs in 13 (2.0%) subjects], Decreased appetite [10

AEs in 6 (0.9%) subjects], Vomiting [5 AEs in 4 (0.6%) subjects], Diarrhea [3 AEs in 2 (0.3%) subjects] and Somnolence [2 AEs in 1 (0.2%) subject].

In another controlled Phase-III (BECT061) study conducted in 300 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the safety profile of BE-PCV14 was comparable to the control vaccine licensed comparator in terms of overall AE rates, related AE rates and medically attended AEs. The most reported adverse events in BE-PCV14 group were Injection site pain [24 AEs in 17 (11.3%) subjects], Injection site swelling [14 AEs in 10 (6.7%) subjects], Injection site erythema [10 AEs in 10 (6.7%) subjects], Irritability post vaccinal [12 AEs in 5 (3.3%) subjects], Pyrexia [5 AEs in 5 (3.3%) subjects] and Injection site induration [1 AE in 1 (0.7%) subject]. The most commonly reported adverse events in licensed comparator group were Injection site pain [25 AEs in 19 (12.7%) subjects], Injection site swelling [16 AEs in 13 (8.7%) subjects], Pyrexia [13 AEs in 12 (8.0%) subjects], Irritability post vaccinal [9 AEs in 6 (4.0%) subjects], Injection site erythema [7 AEs in 7 (4.7%) subjects] and Vomiting [1 AE in 1 (0.7%) subject].

In both the phase III studies, all the reported adverse events were mild to moderate in their intensity and majority of the adverse events were considered related to the study vaccine by the investigators. No AEs that were considered severe in their intensity were reported in either of the treatment groups. Majority of the reported adverse events are solicited in nature. There were no SAEs and deaths reported in the study. No clinically significant changes overtime were noted in the vital signs recorded. The AEs observed and physical examination results did not indicate any safety issues of concern.

4.9 Overdose

No case of overdose has been reported.

There is no specific treatment for an overdose with BE-PCV14. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

BE-PCV14 contains polysaccharides from serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F conjugated to non-toxic diphtheria toxin cross-reacting material (CRM_{197}). The body develops an immune response against the injected serotypes which would help in prevention of disease caused by *Streptococcus pneumoniae*.

5.2 Pharmacodynamic Properties

Streptococcus pneumoniae causes paediatric invasive bacterial disease (including bacteremia, bacterial pneumonia, and meningitis) and is estimated to account for approximately 1 million deaths per year worldwide among children younger than 5 years of age. BE-PCV14 contains polysaccharides from serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F conjugated to non-toxic diphtheria toxin cross-reacting material (CRM_{197}). In the clinical trials conducted in healthy infants, the vaccine was found to be safe and immunogenic.

In a Phase-II (BECT044) comparative study conducted in 120 subjects aged 12-23 months, randomized in 1:1 ratio between BE-PCV14 or 13 valent licensed comparator given as 2 doses with 2 months apart, the proportion of subjects seroconverted after two doses were 96.55% (56), 98.28% (57), 100% (58), 100% (58), 93.10% (54), 100% (58), 100% (58), 100% (58), 100% (58), 98.28% (57), 100% (58), 98.28% (57), 100% (58) and 91.38% (53) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F respectively and has shown comparable immunogenicity with that of licensed comparator.

In a Phase-III (BECT051) study conducted in 1290 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at visit 3 (Day 86) were 90.6% (581), 83.5% (535), 93.1% (597), 90.6% (581), 76.3% (489), 95.8% (614), 95.2% (610), 99.7% (639), 90.5% (580), 99.4% (637), 97.2% (623), 94.1% (603), 82.4% (528)

and 73.2% (469) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F & 33F respectively.

In another Phase-III (BECT061) study conducted in 300 infants of 6-8 weeks old in 6-10-14 weeks dosing schedule, randomized in 1:1 ratio between BE-PCV14 or 13-valent licensed comparator, the proportion of subjects seroconverted at visit 3 (Day 86) were 93.3% (139), 76.5% (114), 91.3% (136), 88.6% (132), 81.2% (121), 96.6% (144), 94.6% (141), 100.0% (149), 91.3% (136), 100.0% (149), 97.3% (145), 88.6% (132), 86.6% (129) and 67.1% (100) against serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F & 33F respectively.

The immune response to serotype 6A was achieved through cross protection from serotype 6B with BE-PCV14, which is evident from two phase III clinical studies.

BE-PCV14 has shown comparable seroconversion rates for the common serotypes of the 13 valent licensed comparator in terms of anti-PnCPS IgG antibody concentrations in all the studies conducted so far.

5.3 Pharmacokinetic Properties

Evaluation of pharmacokinetic properties is not required for vaccines.

5.4 Preclinical Safety Data

Single dose toxicity studies in Rats and repeat dose toxicity studies in Rats and Rabbits were conducted. Based on the toxicity studies conducted, it is concluded that the vaccine formulation did not produce any adverse effects at dose level of 0.5 mL.

Immunogenicity studies are also conducted with the vaccine in Rats and Rabbits. Based on the immunogenicity studies, the vaccine showed IgG response to individual serotypes PnCPS in the vaccine formulation.

6. PHARMACEUTICAL PARTICULARS

The vaccine contains *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F.

6.1 List of Excipients

List of excipients:

- Aluminum Phosphate as Al^{+++}
- 2 Phenoxyethanol (as preservative in multi dose presentation)

Other Ingredients:

- Polysorbate 20
- Succinic Acid

6.2 Incompatibilities

The product should not be mixed with any other medicinal products or active immunizing agents.

6.3 Shelf Life

24 months from the date of manufacturing. The manufacturing date of the vaccine is indicated on the label and carton of the product.

6.4 Special Precautions for Storage

Store at +2°C to +8°C. DO NOT FREEZE. Discard if found frozen. Shake well before use. Keep out of reach of children.

6.5 Nature and Contents of Container

The BE-PCV14 is filled in USP type I glass vials, closed using bromobutyl rubber stoppers and sealed with aluminium flip-off seals.

The vaccine is filled in to single dose and five dose presentation and is offered in the following presentations.

- Single dose vial of 0.5 mL
- Single dose vial of 0.5 mL with Syringe and Needles
- Five dose vial of 2.5 mL.

The above presentations are offered in different packaging configuration as per the requirement. Not all pack sizes may be marketed.

6.6 Instruction for use, handling and disposal

Each vaccine dose of 0.5 mL is withdrawn into a syringe for injection to be administered intramuscularly. Use a separate sterile needle and syringe for each individual.

Handling of multi dose vial: Once opened, multi dose vials of BE-PCV14 from which one or more doses of vaccine have been removed during an immunization session may be used in subsequent immunization sessions for up to a maximum of 28 days, provided that all of the following conditions are met:

- the expiry date has not passed
- the vaccines are stored under appropriate cold chain conditions
- the vaccine vial septum has not been submerged in water
- Aseptic technique has been used to withdraw all doses
- The vaccine vial monitor (VVM) (if attached) has not reached the discard point.

7. MARKETING AUTHORISATION HOLDER

Biological E. Limited

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Manufacturing Site Address:

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8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION

10.12.2022 (INDIA)

10. DATE OF REVISION OF THE TEXT

June 2023